The Quality System Inspection Technique:

“QSIT”

What is QSIT?

• Moves FDA closer to Global Harmonization guideline for regulatory auditing of quality systems of medical device manufacturers
• Incorporates the seven subsystems concept
• Provides specific guidance on auditing each subsystem

Quality System’s Subsystems
Theme #1 = Management

- Management is responsible for Implementing Quality System
- Start & Finish with Management
- All product, process, design & CAPA problems can be tied to management

Theme #2 = CAPA

- We are checking the “system”
  - Non-conformances happen
  - What kind of system does the firm have?
  - Is the system effective?

The Inspection Approach

- Top-down
  - (versus Bottom-up)
- Sampling records
  - (use tables)
- Pre-inspection activities
  - (ask for and review documents)
- Start and end with Management
Establish - [21CFR 820.3(k)]

- Define
- Document
- Implement

The “Establish” Test

- Proof of “Establish”
  - Is the firm doing what regulation says?
  - Is the firm doing what their procedure says?
  - Is the firm doing it adequately?

Order of Systems

- Management
- Design
- CAPA
- Production & Process Controls
- Conclude with Management
Not in the Law

• Preannounced Inspections
  – Call prior to inspection to advise firm of inspection
  – Request copies of Quality Policy and high level Quality System Procedures
• FD-483 Annotation
• Post Inspection Notification

As required by law

• Credentials displayed
• Written Notice of Inspection
• List of Observations
  – FD-483

Preparation

• Assignment
  – Compliance Program
  – Inspectional Guidance
• Past history
  – District files
  – Previous investigator
Preparation

• MDR Database
• Complaints
  – Customer complaints to FDA
  – Trade complaints
• Headquarters
  – 510(k)/PMA reviewers

On-site

• Introductory discussion
  – Purpose of the inspection
  – Rough schedule - time estimate
  – Special needs
    • Firm
    • FDA

On-site

• Overall plant tour
  – Overview of operations
  – Location of key operations
  – Production flow
  – Include offices
On-site

- Complaint file review
  - Numbers of complaints
  - Types of complaints
  - Trends
  - MDR’s

On-site

- Manufacturing operations
  - Start with incoming materials
  - Follow process to completion
  - Look at the details of each process

- Support procedures
  - Calibration
  - Training
  - Change procedures
  - Audit procedures

Record Review

- Device Master Record
- Device History Records
  - Chosen at random
  - Chosen from complaint files
- Incoming Inspection reports
  - may be separate from DHR’s
Record Review

• In-process Inspection reports
  – may be separate from DHR's
• Service records
  – may be included in complaint file review
• Calibration records
• Maintenance records

Close out

• Issue FD-483
  – To most responsible person
  – Listing of problem areas
  – Includes examples

Close out

• Discuss FD-483
  – Has corrective action been initiated?
  – Are issues understood?
  – Is management serious about correction?
  – Will a written response be forthcoming?
Close out

- Discuss other findings
  - Minor problems
  - Areas without problems
    - Was anything being done right?

Post inspection

- Establishment Inspection report
  - Prepared
  - Reviewed
- Follow up assignments
  - Sample collections
  - Investigate complaints or service reports

Post inspection

- Initiate action
  - Warning letter
  - Injunction
  - Seizure
  - Prosecution
Medical Device Reporting
Direct Final Rule
2/28/05

FD&C Act 519
• As amended by:
  – Safe Medical Devices Act of 1990
  – Medical Device Amendments of 1992
  – FDA Modernization Act of 1997
• Authority to require manufacturers, distributors and device user facilities to submit reports on certain types of medical device related adverse events

21 CFR 803.1
• Requirements for medical device reporting
  – device user facilities,
  – manufacturers,
  – importers, and
  – distributors
21 CFR 803.1

• Device user facility:
  – must report deaths and serious injuries that a
device has or may have caused or contributed
to,
  – establish and maintain adverse event files,
  and
  – submit summary annual reports

• Manufacturer or importer:
  – report deaths and serious injuries that their
device has or may have caused or contributed
to,
  – report certain device malfunctions, and
  – establish and maintain adverse event files

• Manufacturer
  – submit specified followup and baseline reports

• Medical device distributor:
  – maintain records (files) of incidents,
  – not required to report these incidents
• Become aware means
  – that an employee of the entity required to report has acquired information that reasonably suggests a reportable adverse event has occurred

• Device user facility:
  – considered to have “become aware” when medical personnel, ..., who are employed by or otherwise formally affiliated with your facility, obtain information about a reportable event.

• Manufacturer:
  – considered to have “become aware” … when any employee becomes aware of a reportable event …
21 CFR 803.3

• Manufacturer:
  – also considered to have become aware of an event when any ... employees with management or supervisory responsibilities over persons with regulatory, scientific, or technical responsibilities, or whose duties relate to the collection and reporting of adverse events, becomes aware, ..., that a reportable MDR event or events necessitates remedial action to prevent an unreasonable risk of substantial harm to the public health.

21 CFR 803.3

• Importer:
  – considered to have "become aware" of an event when any .. employee becomes aware of a reportable event that is required to be reported 30 days

21 CFR 803.3

• Caused or contributed means
  – that a death or serious injury was or may have been attributed to a medical device, or
  – that a medical device was or may have been a factor in a death or serious injury
21 CFR 803.3

- Caused or contributed includes events occurring as a result of:
  - Failure;
  - Malfunction;
  - Improper or inadequate design;
  - Manufacture;
  - Labeling; or
  - User error.

21 CFR 803.3

- Device user facility means
  - a hospital, ambulatory surgical facility, nursing home, outpatient diagnostic facility, or outpatient treatment facility …,
  - which is not a physician's office, ….
  - School nurse offices and employee health units are not device user facilities.

21 CFR 803.3

- Distributor means
  - any person (other than the manufacturer or importer) who furthers the marketing of a device from the original place of manufacture to the person who makes final delivery or sale to the ultimate user, but
  - who does not repack or otherwise change the container, wrapper, or labeling of the device or device package.
21 CFR 803.3

• Hospital means
  – a distinct entity that operates for the primary purpose of providing diagnostic, therapeutic (such as medical, …), surgical, and other patient services for specific and general medical conditions.
  – Hospitals include general, chronic disease, rehabilitative, psychiatric, and other special-purpose facilities.

21 CFR 803.3

• Importer means
  – any person who imports a device into the United States and
  – who furthers the marketing of a device from the original place of manufacture to the person who makes final delivery or sale to the ultimate user, but
  – who does not repack or otherwise change the container, wrapper, or labeling of the device or device package

21 CFR 803.3

• Manufacturer means
  – any person who manufactures, prepares, propagates, …a device by chemical, physical, biological, or other procedure.
21 CFR 803.3

- Including any person who either:
  - Repackages or otherwise changes the container, wrapper, or labeling of a device in furtherance of the distribution of the device from the original place of manufacture;
  - Initiates specifications for devices that are manufactured by a second party for subsequent distribution by the person initiating the specifications;
  - Manufactures components or accessories that are devices …; or
  - Is the U.S. agent of a foreign manufacturer.

21 CFR 803.3

- MDR reportable event (or reportable event) means:
  - An event that user facilities become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury; or

21 CFR 803.3

- MDR reportable event (or reportable event) means:
  - An event that manufacturers or importers become aware of that reasonably suggests that one of their marketed devices:
    - May have caused or contributed to a death or serious injury, or
    - Has malfunctioned and that the device … would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.
21 CFR 803.3

• Serious injury means an injury or illness that:
  – Is life-threatening,
  – Results in permanent impairment of a body function or permanent damage to a body structure, or
  – Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

21 CFR 803.10

• Device user facility,
  – Submit reports of individual adverse events no later than 10 work days after the day that you become aware of a reportable event:
    • Submit reports of device-related deaths to FDA and to the manufacturer, if known; or
    • Submit reports of device-related serious injuries to the manufacturers or, ...
  – Submit annual reports

• Importer,
  – Submit reports of individual adverse events no later than 30 calendar days after the day that you become aware of a reportable event:
    • Submit reports of device-related deaths or serious injuries to FDA and to the manufacturer; or
    • Submit reports of device-related malfunctions to the manufacturer.
21 CFR 803.10

• Manufacturer,
  – Submit reports of individual adverse events no later than 30 calendar days after the day that you become aware of a reportable death, serious injury, or malfunction.

21 CFR 803.10

• Manufacturer,
  – Submit reports of individual adverse events no later than 5 work days after the day that you become aware of:
    • A reportable event that requires remedial action to prevent an unreasonable risk of substantial harm to the public health, or
    • A reportable event for which FDA made a written request.
  • See 21 CFR 803.53

21 CFR 803.10

• Manufacturer,
  – Submit annual baseline reports.
  – Submit supplemental reports if you obtain information that you did not submit in an initial report.
21 CFR 803.20

• Information that reasonably suggests that a reportable event has occurred
  – Any information, including professional, scientific, or medical facts, observations, or opinions, may reasonably suggest that a device has caused or may have caused or contributed to an MDR reportable event.

21 CFR 803.20

• You do not have to report an adverse event if you have information that would lead a person who is qualified to make a medical judgment reasonably to conclude that a device did not cause or contribute to a death or serious injury, or that a malfunction would not be likely to cause or contribute to a death or serious injury if it were to recur.
  – Persons qualified to make a medical judgment include physicians, nurses, risk managers, and biomedical engineers.
  – You must keep in your MDR event files the information that the qualified person used to determine whether or not a device-related event was reportable.

Manufacturer reporting requirements

• What information must be submitted:
  – Any information that you can obtain by contacting a user facility, importer, or other initial reporter;
  – Any information in your possession; or
  – Any information that you can obtain by analysis, testing, or other evaluation of the device.
Manufacturer reporting requirements

• Manufacturers are responsible for obtaining and submitting information that is incomplete or missing from reports submitted by user facilities, importers, and other initial reporters.
• Manufacturers are responsible for conducting an investigation of each event and evaluating the cause of the event.
  – If complete information cannot be submitted, you must provide a statement explaining why this information was incomplete and the steps you took to obtain the information.
  – Information obtained after the initial report is filed must be submitted in a supplemental report under Sec. 803.56

Manufacturer reporting requirements

• Information to be submitted:
  – Patient information (Form 3500A, Block A).
    • Patient name or other identifier;
    • Patient age at the time of event, or date of birth;
    • Patient gender; and
    • Patient weight.
  – Adverse event or product problem (Form 3500A, Block B).
    • Identification of adverse event or product problem;
    • Outcomes attributed to the adverse event (e.g., death or serious injury);
    • Date of event;
    • Date of report by the initial reporter;
    • Description of the event or problem,
    • Description of relevant tests, including dates and laboratory data; and
    • Other relevant patient history including preexisting medical conditions.

Manufacturer reporting requirements

• Information to be submitted:
  – Device information (Form 3500A, Block D).
    • Brand name;
    • Type of device;
    • Your name and address;
    • Operator of the device (health professional, patient, ...);
    • Expiration date;
    • Model number, catalog number, serial number, lot number, or other identifying number;
    • Date of device implantation (month, day, year);
    • Date of device explantation (month, day, year);
    • Whether the device was available for evaluation, and whether the device was returned to you, and if so, the date it was returned to you; and
    • Concomitant medical products and therapy dates.
Manufacturer reporting requirements

- Information to be submitted:
  - Initial reporter information (Form 3500A, Block E).
    - Name, address, and phone number of the reporter who initially provided information
    - Whether the initial reporter is a health professional;
    - Occupation; and
    - Whether the initial reporter also sent a copy of the report to FDA
  - Reporting information for all manufacturers (Form 3500A, Block G).
    - Your reporting office’s contact name and address and device manufacturing site;
    - Your telephone number;
    - Your report sources;
    - Date received by you (month, day, year);
    - Type of report being submitted (e.g., 5-day, initial, followup); and
    - Your report number.

- Device manufacturer information (Form 3500A, Block H).
  - Type of reportable event (death, serious injury, malfunction, etc.);
  - Type of followup report, (correction, response to FDA request, etc);
  - Evaluation of the device involved;
  - Device manufacture date (month, day, year);
  - Whether the device was labeled for single use;
  - Evaluation codes;
  - Whether remedial action was taken and the type of action;
  - Whether the use of the device was initial, reuse, or unknown;
  - Whether remedial action was reported as a removal or correction and if it was, provide the correction/removal report number; and
  - Your additional narrative; and/or
  - Corrected data.

Baseline Reports

- You must submit a baseline report for a device when you submit the first report under Sec. 803.50 involving that device model.
- You must update each baseline report annually on the anniversary month of the initial submission, after the initial baseline report is submitted.
International Organization for Standardization
ISO

ISO
• National Standards bodies of 91 countries
  –American National Standards Institute (ANSI) represents US
• 180 Technical Committees
  –Each responsible for an area of specialization

ISO 9000
• Series of documents
  –5 individual, related international standards on quality management and quality assurance
• Applicable to any industry
ISO 9000

• Non-regulatory
  – ISO 9000 registration may be an alternative for product certification in some countries
• Quality system registered or approved
  – assessment and audit by quality system registrar (accredited 3rd party)
  – Quality system registrar issues a “certificate of registration”

ISO 9000

• Quality Management and Quality Assurance Standards - Guidelines for Selection and Use
  – Fundamental quality concepts
  – Definitions of key terms
  – Guidance on selecting, using and tailoring ISO-9001, 9002, 9003 to specific operations

ISO 9001

• Quality Systems - Model for Quality Assurance in Design / Development, Production, Installation and Servicing
  – Most comprehensive standard
  – Covers all elements listed in ISO-9002 and 9003
  – Addresses design, development and servicing capabilities
ISO 9002
• Quality Systems - Model for Quality Assurance in Production and Installation
  –Prevention, detection and correction of problems during production and installation

ISO 9003
• Quality Systems - Model for Quality Standard
  –Requirements for the detection and control of problems during final inspection and testing

ISO 9004
• Quality Management and Quality System Elements – Guidelines
  Guidance for suppliers in development and implementation of a quality system
  –Determining the extent to which each quality element is applicable
ISO 9004

- Quality Management and Quality System Elements - Guidelines
  - Examines each quality system element
  - Cross references in the other ISO-9000 standards
  - Can be used for internal and external auditing

ISO 13485

- ISO 13485:2003 Medical devices -- Quality management systems -- Requirements for regulatory purposes
- International standard
  - Specifies requirements for regulatory purposes for medical device manufacturers
  - Harmonized model for quality management system requirements in the international market

ISO 13485

- Systemic requirements
  - Establish a Quality System
  - Document the Quality System
- Management Requirements
  - Support Quality
  - Establish a Quality Policy
  - Carry out Management Reviews
ISO 13485

• Resource requirements
  – Provide Quality Resources
  – Provide Quality Personnel
  – Provide Quality Infrastructure
  – Provide Quality Environment

• Realization Requirements
  – Control Product Design and Development
  – Control Purchasing
  – Manage Production and Service

ISO 13485

• Remedial Requirements
  – Monitor and Measure Quality
  – Control Nonconforming Products
  – Analyze Quality Information
  – Take Required Remedial Actions